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ALBERTA DIGESTIVE DISEASE SUMMIT
Dysplasia Screening in Ulcerative Colitis: Have we been doing it wrong all these years?

June 7th, 2014

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Outline

1. UC cancer risk
2. UC dysplasia risk and outcomes
3. Current practice vs Guidelines
4. Chromoendoscopy: What, How and Why
5. Chromoendoscopy: Practical application
6. Surface guidelines
7. Dysplasia Management

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Disclosure

None

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Colon Cancer Risk in Ulcerative Colitis (UC)

- An established complication of UC with rates as high as 30% at 35 years of disease
- Newer data has shown this rate to be much lower, however still present
- The mechanisms is thought to be an inflammatory driven process
- The lesions are detectable by endoscopy ranging from low grade to malignancy

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Risk Factors

TABLE 1. Factors that Alter the Risk of CRC in IBD

Risk Factor	RR (95% CI)	
Extent of colonic involvement		
Pancolitis	14.8 (11.4-18.9	Ekbom A, et al, *N Engl J Med.* 323, 1228 (1990)[9]
Left-sided disease	2.8 (1.6-4.4)	
Proctitis	1.7 (0.8-3.2)	
Primary sclerosing cholangitis	OR 4.8 (3.9-6.4)[a]	Soetikno RM, et al, *Gastrointest Endosc.* 56, 48 (2002)[10]
Family history of sporadic CRC		Askling J, et al, *Gastroenterology.* 120, 1356 (2001)[11]
First-degree relative > 50 yr	2.5 (1.4-4.4)	
First-degree relative < 50 yr	9.2 (3.7-23.0)	
Stricture	5.7 (1.7-18.9)	Rutter MD, et al, *Gut.* 53, 1813 (2004)[12]
Inflammatory pseudopolyps	2.1 (1.2-3.7)	Rutter MD, et al, *Gut.* 53, 1813 (2004)[12]
Sex		Soderlund S, et al, *Gastroenterology.* 138, 1697 (2010)[13]
Male	1.6 (1.2-2.2)	
Histological inflammation		
OR 4.7 per unit increase on 0–4 scale		Rutter M, et al, *Gastroenterology.* 126, 451 (2004)[14]
HR 3.0 (1.4–6.3) per unit increase in mean score on 0–3 scale		Gupta RB, et al, *Gastroenterology.* 133, 1099 (2007)[15]

Inflammatory Bowel Disease. Volume 19, Issue 4. 2013.

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Outcomes

Dysplasia	Probability of Cancer at Immediate colectomy	5 years progression to cancer	Surveillance
Negative	1.1%	4% in 10 years	1-2 years
Indefinite	9%	Repeat within 3-6 months	
Flat LGD	16-34%	16-54%	Accelerated surveillance
Flat HGD	42-67%	25-32%	Colectomy
DALM (non-resectable)	31-65%	Colectomy	

Best Practice and Research Clinical Gastroenterology Volume 27, Issue 2, April 2013

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Colonoscopic surveillance

- Current paradigm that exists follows decreasing interval colonoscopy with targeted and (~32) random biopsies
- 33 random biopsies giving yield of 90% for dysplasia, derived from evidence of large field defects with in the epithelium[1]
- These were field defects thought to give rise to dysplasia

Rubin et al. Gastroenterology 1992

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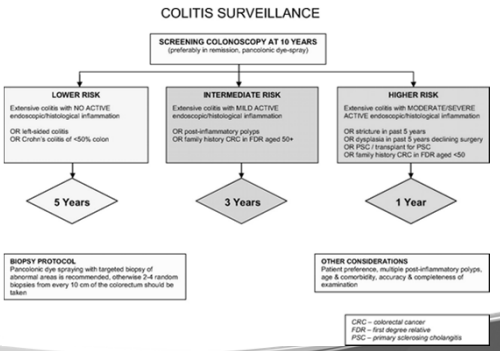

Cairns S R et al. Gut 2010;59:666-689

GUT

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Random biopsy

- 10 prospective studies using quadratic random biopsy protocol have been published
- 1 episode of dysplasia for every 1505 random biopsies
- Assuming a 1cm patch of dysplasia 320 biopsies would be needed for random pick up

Riddell et al. Clinical Gastroenterology and Hepatology. 2014

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Chromoendoscopy

- Application of a chemical substance to the gastrointestinal mucosa to enhance the visualization of different types of epithelia to aid in the detection of subtle dysplastic and neoplastic lesions
- Stains:
  1. Vital – absorbed into the mucosa
  2. Contrast –pool on the surface
  3. Reactive – react with the underlying mucosa tissue type

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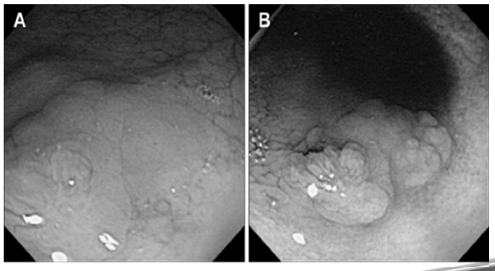
Methylene Blue



Gut and Liver, Vol. 2, No. 2, September 2008

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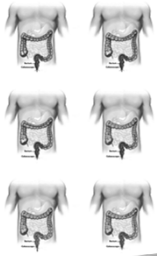
Chromoendoscopy in UC dysplasia

- Prospective trial
- 102 pts : 79 UC, 23 CD
  All patients underwent double pass endoscopy
- Segmental White light (WL) with random biopsy and targeted
- Chromoendoscopy targeted (CE)



Marion et al. American Journal of Gastroenterology, 2008.

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Outcomes

	LGD	IGD	HGD	TDD	Total Biopsy	Yield %
Random WL	3	16	0	19	3264	0.5%
Targeted WL	12	2	1	15	50	30.0%
Targeted CE	21	13	1	34	82	41.5%

LGD Low grade dysplasia
IGD Indeterminant dysplasia
HGD High grade dysplasia
TDD Total detected dysplasia

Marion et al. American Journal of Gastroenterology. 2008.

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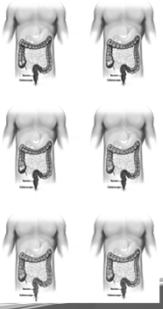
Procedure

- Scope passage to the cecum
- 2 amps of methylene blue in 500cc of sterile water placed in the jet wash
- On withdrawal of the scope the colon is segmentally (20 – 30cm) dyed
- Areas of absent dye uptake and mucosal irregularity should be inspected and biopsied\removed



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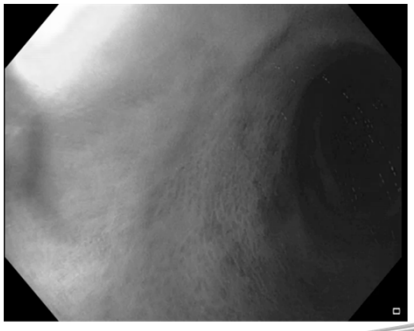

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SURFACE Guidelines

1. **S**trict Patient Selection
2. **U**nmask the mucosal surface
3. **R**educe peristalsis
4. **F**ull length staining
5. **A**ugment with dies
6. **C**rypt architecture analysis (pit III – V)
7. **E**ndoscopic targeted biopsy

Kiesslich. Gut 2004

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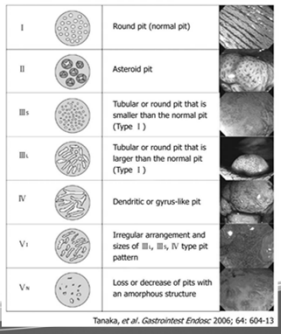
Pit Pattern Assessment



Tanaka, *et al. Gastrointest Endosc* 2006; 64: 604-13

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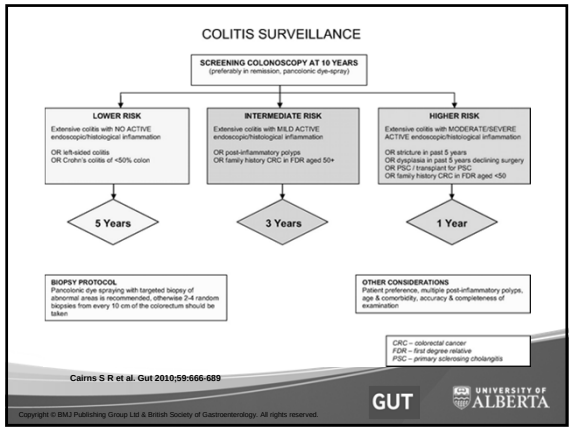

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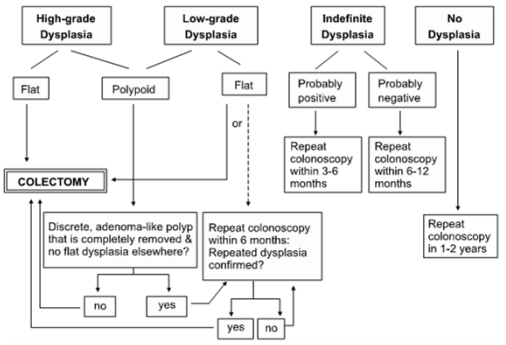

Gut and Liver, Vol. 2, No. 2, September 2008

Take home

1. **Dysplasia and Malignancy is an established complication of UC**
2. **The previous concepts of "invisible" or flat dysplasia has changed**
3. **Screening regimens should be tailored to the patient via updated guidelines**
4. **The current data supports the use of chromoendoscopy with targeted biopsies for dysplasia detection**
5. **Management of dysplasia now becomes controversial**

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